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Gene expression profiling of H9c2 myoblast differentiation towards a cardiac-like phenotype

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Abstract

 H9c2 myoblasts are a cell model used as an alternative for cardiomyocytes. H9c2 cells have the ability to differentiate towards a cardiac phenotype when the media serum is reduced in the presence of all-tran--retinoic acid (RA), creating multinucleated cells with low proliferative capacity. In the present study, we performed for the first time a transcriptional analysis of the H9c2 cell line in two differentiation states, i.e. embryonic cells and differentiated cardiac-like cells. The results show that RA-induced H9c2 differentiation increased the expression of genes encoding for cardiac sarcomeric proteins such as troponin T, or calcium transporters and associated machinery, including SERCA2, ryanodine receptor and phospholamban as well as genes associated with mitochondrial energy production including respiratory chain complexes subunits, mitochondrial creatine kinase, carnitine palmitoyltransferase I and uncoupling proteins. Undifferentiated myoblasts showed increased gene expression of pro-survival proteins such as Bcl-2 as well as cell cycle-regulating proteins. The results indicate that the differentiation of H9c2 cells lead to an increase of transcripts and protein levels involved in calcium handling, glycolytic and mitochondrial metabolism, confirming that H9c2 cell differentiation induced by RA towards a more cardiac-like phenotype involves remodeled mitochondrial function. PI3K, PDK1 and p-CREB also appear to be involved on H9c2 differentiation. Furthermore, complex analysis of differently expressed transcripts revealed significant up-regulation of gene expression related to cardiac muscle contraction, dilated cardiomyopathy and other pathways specific for the cardiac tissue. Metabolic and gene expression remodeling impacts cell responses to different stimuli and determine how these cells are used for biochemical assays.

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